

Application No.: 10/804,915

Attorney Docket No. A-846 (US)

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**I. The Newly Set Forth Restriction Requirement**

The Office Action sets forth, for the first time, the Examiner's self-determined "scope of the independent invention" (assertedly created based solely upon the previous election of a single species) which – in the terms employed by the Office Action – forms the basis of a new Restriction Requirement. There are a number of objectionable aspects to the Examiner's new Restriction Requirement:

- The Examiner has failed to set forth a clear intelligible "scope of the invention" that would allow Applicants to submit a reasoned response that could thoroughly address all points raised in the Office Action.
- The Examiner's self-determined "scope of the independent invention" is extremely overly narrow, and examination of a significantly enlarged scope would not seriously burden the Examiner. Moreover, the procedure outlined in MPEP § 803.02 mandates that the scope of examination be expanded in some fashion, because the examination of the initial scope uncovered no prior art raising issues of unpatentability.
- The Office Action faults Applicants for not previously providing any rebuttal arguments to the substance of the new Restriction Requirement – which had never before been presented to the Applicants for review/rebuttal.

Applicants respectfully submit that these points (which are addressed in more detail below in sections I.A through I.C) thoroughly support traversal of the Examiner's new Restriction Requirement. Accordingly, Applicants request that the Examiner withdraw the current Restriction, and reissue a Restriction that is more in line with that proposed below in section I.B.

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**A. The New Restriction Requirement Is Unclear And Does Not Allow Applicants To Submit a Complete, Reasoned Response**

The new basis for Restriction is unclear and generates a number of ambiguities/inconsistencies, which prevent Applicants from submitting a full, clear response, which would address all points raised by the Examiner. This violates the provisions of MPEP § 814, which states: "The examiner must provide a clear and detailed record of the restriction requirement to provide a clear demarcation between restricted inventions..." (emphasis in original)

The first aspect of unclarity raised by the new grounds for Restriction is that the Examiner appears to specifically limit Applicants to claiming compounds of "formula III" - which suggests that the Examiner might be intending to require Applicants to withdraw the subject matter of claims 1-44 in their entirety (as "formula III" only first appears in claim 45) - though neither the Office Action, nor Form PTOL-326 specifically indicates this. Stated another way, it is unclear whether the Examiner intends to allow Applicants to pursue claims (otherwise limited by considerations of a proper Restriction) which would utilize either of the terms "formula I" or "formula II". For example, Applicants present herewith amended claims that utilize the terms "formula I" and "formula II", but which have been otherwise limited in a way which Applicants believe represent a fair scope of Restriction (see section I.B.ii, below). The mere fact that Applicants would employ the terms "formula I" and "formula II" should not matter from a substantive view point. However, the new Restriction Requirement appears to specifically limit Applicants to claiming compounds of "formula III" (i.e., claim 45). Applicants submit that rather than restrict the claims in terms of a specific formula, it would have been clearer if the Examiner had simply restricted the claims in terms of definitions set forth in claim 1 (e.g., a restriction to compounds where ring "A" is phenyl, Y<sup>1</sup> is nitrogen, Y<sup>2</sup> is oxygen, dashed line "a" is absent and dashed line "b" is a bond -- see also, section I.B.ii, below).

The second aspect of unclarity raised by the new grounds for Restriction is that the initial language employed by the Restriction provides:

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$R_1''$  is H,

$R_1$  and  $R_1'$  are the same or different and are F,  $\text{NO}_2$ , CN, Cl,  $\text{CHF}_2$ ,  $\text{CF}_3$ ,  $-\text{NR}_7\text{R}_8$  or  $-\text{OR}_9$  .... (Office Action, page 2, lines 14-15).

However, nowhere in the claims or specification are the variables  $R_1''$ ,  $R_1$  or  $R_1'$  even described or used, and Applicants can discern no other variables that are actually employed which might possibly correspond to the variables  $R_1''$ ,  $R_1$  or  $R_1'$  which have been set forth in the new Restriction Requirement.

The third aspect of unclarity is that the Office Action, as well as Form PTOL-326, indicates that claim 22 has been withdrawn from consideration (presumably on the basis that it is drawn to non-elected subject matter). However, claim 22 only contains a provision which limits variable X to being NH. Confusion is thus caused for two reasons: (1) the new Restriction Requirement contains no specific limitation directed to the definition of variable X; and (2) even assuming, arguendo, that the Examiner implicitly intended to limit variable X by limiting the invention to compounds of "formula III" (which is itself unclear to begin with – see section I.A, above) a compound where X is NH would be, in any event, entirely within the scope of "formula III".

#### **B. The Restriction Requirement is Overly Narrow**

The new Restriction Requirement is overly narrow, and the Examiner has failed to adequately support the basis for this extremely narrow restriction -- in particular, the bases for the restrictions directed to variables  $R$ ,  $R^{1a}$ ,  $R^2$ ,  $R^3$  and  $R^6$ . Also, the examination of a significantly expanded claim scope (e.g., one that is limited to a central benzoxazole core/scaffold, as suggested below in section I.B.ii.) would provide for a "unified" scope of invention, and would not seriously overburden the Examiner. Moreover – regardless of what is ultimately determined to be the proper scope of examination – under the procedure for examining Markush claims that are subject to restriction, which is outlined in MPEP § 803.02, the Examiner is obligated to expand the scope of examination in some fashion, because the examination of the initial scope uncovered no prior art raising issues of unpatentability.

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**i. The Examiner has failed to support  
the basis for the narrow restriction**

The Examiner bears the initial burden of providing an adequate explanation for supporting the basis of a restriction.. As reflected in MPEP § 814:

"The examiner must provide a clear and detailed record of the restriction requirement to provide a clear demarcation between restricted inventions..."  
(emphasis in original)

Additionally, in cases such as this where an application claims plural species MPEP § 806.04(h) provides:

"In making a requirement for restriction in an application claiming plural species, the examiner should group together species considered clearly unpatentable over each other." (emphasis added).

Yet, in this case the Examiner has failed to explain why any withdrawn subject matter is allegedly patentably distinct over the examined subject matter (or stated conversely – in the terms used in MPEP § 806.04(h) – why the examined (restricted) subject matter is "clearly unpatentable over each other"). Applicants wish to stress that nothing in this response should be construed as an argument that the withdrawn subject matter is patentably indistinct from the examined subject matter. Rather, Applicants are simply asserting that it is not appropriate for the Examiner to merely set forth an unsupported restriction (i.e., simply state the conclusion) and then require that, in order to traverse the requirement that Applicants present evidence contradicting a position that has never been articulated in the first instance.

As far as Applicants can discern, the only support that the Examiner attempts to provide for this overly narrow restriction is that various withdrawn moieties (covered by certain distal fragments of formulae I, II and III) are structurally diverse. Specifically, the Examiner states:

"The above mentioned withdrawn compounds which are withdrawn from consideration as being for non elected subject matter differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds differ from those of the elected invention such as by, tetrazolyl,

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diazolyl, triazolyl, perazine, piperidine, morpholine, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the compounds can be seen by the various classification of these compounds in the U.S. classification system...." (Office Action at page 3, lines 12-18). But this position, however, is primarily directed to concerns of "unity of invention" and/or "serious burden of examination" (which are addressed separately below in section I.B.ii) rather than the issue of patentable distinctness. Applicants thus respectfully submit that the Examiner has failed to adequately support a position that the withdrawn subject matter is patentably distinct from the examined subject matter.

**ii. Examination of a claim scope limited to a central  
benzoxazole core would not seriously unburden the Examiner**

Applicants respectfully submit that the examination of a significantly enlarged scope of invention would still result in a "unified" invention that would not cause serious burden to the Examiner. Applicants suggest that a reasonable restriction would allow for the examination of claims wherein (in terms of claim 1) ring "A" is phenyl, Y<sup>1</sup> is nitrogen, Y<sup>2</sup> is oxygen, dashed line "a" is absent and dashed line "b" is a bond -- in other words, a restriction limiting examination to compounds which possess a central benzoxazole core/scaffold. Applicants have herein amended the claims to be consistent with this suggested restriction, and submit that further examination on this suggested scope is proper.

Generally, where claims set forth a "unified" scope of invention, they should be examined without requiring restriction. As stated in MPEP § 803.02:

"[I]t is improper for the Office to refuse to examine that which applicants regard as their invention, ***unless the subject matter in a claim lacks unity of invention.*** Broadly, unity of invention exists where compounds included within the a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility."

Applicants submit that the scope of their suggested restriction presents the Examiner with a "unified" invention because all compounds covered by the claims share a common utility, and further share a substantial common structural feature essential to

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that utility (i.e., a central benzoxazole core/scaffold). Accordingly, "it [would be] improper for the Office to refuse to examine" this subject matter. MPEP § 803.02.

Applicants further submit that the search and examination of the proposed central benzoxazole scaffold now covered in formulae I, II and III, could be made without serious burden on the part of the Examiner. Accordingly, even if a position of patentable distinctness could be properly supported, the Examiner would nonetheless be obligated to conduct this search and examination:

"If the search and examination of all the claims in an application can be made without serious burden, ***the examiner must examine them on the merits***, even though they include claims to independent or distinct inventions." MPEP § 803 (emphasis added).

While the Examiner appears to be taking the position that various structural diversities between distal fragments of compounds covered by the claimed invention would require differing classification in the U.S. classification system, and thus (presumably/implicitly) would require an unduly burdensome search (see Office Action at page 3, lines 12-21), Applicants submit that the claimed subject matter is fairly classified in a single class -- i.e., benzoxazoles. Accordingly, a search in this single class should uncover all relevant prior art.

**iii. The procedure outlined in MPEP § 803.02 mandates that the scope of examination be expanded in some fashion**

Regardless of what actual scope of examination is ultimately determined to be proper in this case, the provisions of MPEP § 803.02 (which outlines the procedure for examining Markush claims which have been restricted) mandate that the Examiner expand the scope of examination in some fashion, because examination of the initial scope uncovered no prior art that raised issues of unpatentability. As clearly set forth in MPEP § 803.02:

"Following election (of a species), the Markush-type claim will be examined fully with respect to the elected species ***and further to the extent necessary to determine patentability***. If (following examination with respect to the elected species) the Markush-type claim is not allowable, the provisional election will be

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given effect and examination will be limited to the Markush-type claim and claims to the elected species... On the other hand, should the examiner determine that the elected species is allowable, the examination of the Markush-type claim **will be extended**." (emphases added).

The MPEP provides the Examiner with no discretion on this point. If the initial examination fails to uncover prior art rendering the claims unpatentable, the scope of examination "will be extended". MPEP § 803.02.

Indeed, as clearly reflected in the provision of MPEP § 803.02, the entire practice of requiring the election of a single species in the course of examining Markush claims that have been restricted, is intended to simply address the scope of the initial search conducted by the Examiner, rather than to require a further/additional formal "restriction" of the Markush claims – as has been apparently done here by the Examiner.

Applicants thus respectfully submit that the Examiner is in error to couch the scope of the initial search as an additional formal restriction of the claims – particularly where the initial search uncovers no prior art that would render the claims unpatentable.

**C. The Examiner Faults Applicants For Failing to Respond to a Position That Had Never Before Been Raised**

Before the receipt of the most recent Office Action, Applicants had never been advised of the specific "scope of the independent invention" that was independently generated by the Examiner in view of the elected species. Yet, after setting forth this scope, for the first time, the Examiner proceeds to suggest that Applicants may be somehow estopped from objecting for failure to present arguments contradicting the position:

"Nowhere do applicants argue to the contrary. Nowhere do applicants point out and give reasons why the claims do not involve Independent or distinct subject matter." (Office Action, page 4, lines 3-5).

Clearly, from a procedural standpoint it is improper for the Examiner to require Applicants to rebut a position that has never even been previously presented to them for consideration. Applicants are not in a position to intuit what arguments the Examiner

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will present in the future, and thus cannot provide rebutting evidence/argument in advance of the fact.

## **II. The Objections Raised By The Examiner**

The Examiner has objected to claim 50 as being in improper form for being a multiple dependent claim that does not refer back to claims in the alternative. Applicants have herein amended claim 50 in the manner suggested by the Examiner in order to overcome the objection.

The Examiner has objected to claim 45 on the basis of a formality wherein the variable "R<sup>1</sup>" found on line 22 of the claim on page 274 should properly read "R<sup>1a</sup>". Applicants have amended the claim to replace "R<sup>1</sup>" with "R<sup>1a</sup>", as suggested by the Examiner, in order to overcome the objection.

## **III. The Rejections Under 35 U.S.C. § 112**

The Examiner has rejected claims 1-21, 24, 25, 30-38, 40 and 43-50 under 35 U.S.C. § 112 as being indefinite based on the use of the phrase "pharmaceutically acceptable derivatives thereof" -- the Examiner asserting that the term "derivative" is indefinite. Applicants have herein amended claims 1, 19, 33, 37-42 and 45 to replace the phrase "pharmaceutically acceptable derivatives thereof" with the phrase "enantiomers, diastereomers and pharmaceutically acceptable salts and solvates thereof". Applicants have additionally amended claims 18 and 44 to replace the term "derivatives" with the terms "salts and solvates". Support for the inclusion of "enantiomers and diastereomers" within the scope of the claimed invention can be found in the specification at page 84, lines 19-24. Support for the inclusion of "salts" within the scope of the claimed invention can be found in the specification at page 46, lines 33-34. And support for the inclusion of "solvates" within the scope of the claimed invention can be found in the specification at page 83, lines 4-7. Accordingly, Applicants respectfully submit that these amendments introduce no new matter. Withdrawal of the rejection is respectfully requested.



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The Examiner has rejected claim 45 under 35 U.S.C. § 112 as being indefinite on the basis that variable "R<sup>4</sup>" has no antecedent basis. Applicants have herein amended claim 45 to delete reference to variable "R<sup>4</sup>", thereby obviating the rejection.

The Examiner has rejected claims 1-21, 24, 25, 30-38, 40 and 43-50 under 35 U.S.C. § 112 as being indefinite on the basis that the formulae of the claims contain one variable "R<sup>2</sup>", yet the claim limitations also provide that "R<sup>2</sup> is one or more substituents...". The Examiner asserts that this renders the claims indefinite as to how one variable R<sup>2</sup> is also more than one substituent, and further unclear as to just how many more R<sup>2</sup> variables may be present. Applicants respectfully submit that the rejection is not proper in that one of ordinary skill in the art would understand that the variable R<sup>2</sup> is intended to define one or more optional substituents that may be present at any location on the central fused phenyl ring – limited in number to that which would be allowed by valence (i.e., not exceeding 3). Accordingly, the claims would not be indefinite to one of ordinary skill in the art, and Applicants request that the Examiner withdraw the rejection.

The Examiner has rejected claims 1-21, 24, 25, 30-38, 40 and 43-50 under 35 U.S.C. § 112 as being indefinite on the basis that claims include the use of the terms "contains" and "comprising", which – the Examiner asserts – are open ended terms that can never properly be employed in patent claims directed to chemical compounds. Applicants respectfully submit that the rejection is improper on the following grounds:

- Claim 1, as originally presented, provided that ring A "optionally *contains* a nitrogen atom independently at position 4, 6 or 7". While Applicants submit that the use of the word "contains" in this context is not unduly open-ended and is not contrary to any tenet of Patent Law directed to the use of the word "contains", the point is mooted by the fact that the definition of ring A has been herein limited to phenyl, based on the restriction requirement.
- Claims 19, 28, 30, 33, 39 and 45 employ terms such as "nitrogen-containing heteroaryl" and "nitrogen-containing partially saturated heterocycl". While the Examiner contends that the use of the word "contains" is per se improperly "open-ended", Applicants point

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out that the term "nitrogen-containing heteroaryl" is actually narrower in scope than the simple term "heteroaryl" (and the same is true with respect to "nitrogen-containing partially saturated heterocycl" when compared to the simple term "heterocycl"). It is unclear how these terms can be both narrower than allowable terms, and yet unduly "open-ended". The whole premise underlying the rejection is thus not even supported when the context of the use of the word "contains" within the claims is actually examined.

- Claim 50 is a pharmaceutical composition claim, which provides that the composition "comprises" a pharmaceutically-acceptable carrier and a compound as in any one of claims 1-49. This is standard language employed for pharmaceutical composition claims. Contrary to the position taken by the Examiner, this claim is not directed simply to a chemical compound, but rather is directed to a more complex *composition*, and thus use of the term "comprises" violates absolutely no tenet of Patent Law.
- Claim 11, as originally presented, employed the phrase "heteroaryl *comprising* one or more nitrogen atoms". While Applicants assert that there is nothing improper with this use of the term "comprising", claim 11 has been herein amended to replace the term "comprising" with term "containing" -- in order to employ language that is more internally consistent with that used in claims 19, 28, 30, 33, 37 and 45 (discussed in the second bullet point above). Applicants assert that this change in language does not affect the scope of the limitation.

Moreover, in addition to the points raised above, Applicants note that the Examiner cites absolutely no authority for the asserted broad blanket proposition that the terms "contains" and "comprising" can never properly be employed, in any manner, in patent claims directed to chemical compounds. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

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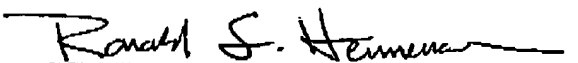
**IV. The Double-Patenting Rejection**

The Examiner has provisionally rejected claims 1-9, 11-17, 19-21, 24, 30-34, 36-38, 40, 43, 45, 46 and 48-50 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 and 42 of co-pending Application Serial No. 11/042,398. As this rejection is provisional in nature, Applicants defer responding to the rejection until such time as any claim(s) actually issue from Application Serial No. 11/042,398 that would purportedly support the rejection.

**V. Conclusion**

For the reasons set forth above, Applicants request that the Examiner expand the scope of examination to encompass the subject matter set forth in the amended claim set provided herewith. In the alternative, Applicants request that the Examiner expand the scope of the search in some fashion in order to comply with the provisions of MPEP § 803.02. Applicants further request that the Examiner refrain from couching the "scope of search" conducted under MPEP § 803.02 in terms of an additional formal "restriction".

Respectfully Submitted,

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Ronald S. Hermenau, Reg. No. 34,620  
Attorney for Applicants  
AMGEN INC.  
1120 Veterans Boulevard  
South San Francisco, CA 94080  
Phone: (650) 244-2261  
Fax: (650) 244-2392